REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 1-10 and 19-42 are pending after entry of the amendments set forth herein.

Claims 1-10 and 19-24 were examined. Claims 1, 4-7, and 9-12, were rejected, and Claims 2, 3, 8-10, 23, and 24 were objected to.

Claims 1, 7 and 22 have been amended. Support for these amendments is found throughout the specification, as well as in the claims as originally filed, at for example: Claim 1: page 15, paragraph 68 through page 16, paragraph 71; Claim 7: page 17, paragraph 73; and Claim 22: page 18, paragraph 79 through page 19, paragraph 81.

Claims 25-42 have been added. Support for new Claims 25-43 is found throughout the specification, as well as in the claims as originally filed, at for example: Claims 25-31: page 18, paragraph 77, page 19, paragraph 80, and page 34, paragraph 132 through page 35, paragraph 133; page 34, paragraph 132; Claims 32-37: page 34, paragraph 132 through page 38, paragraph 141; and Claims 38-42: page 19, paragraph 82, page 21, paragraph 88; page 31, paragraph 122, through page 32, paragraph 124.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

No new matter has been added.

Allowable Subject Matter

Applicants wish to extend their gratitude to the Examiner for indicating that claims 8-10 and 23-24 are directed to allowable subject matter.

Rejections Under §102(e)

Claims 1, 4-7, and 19-22 have been rejected under 35 USC § 102(e), as allegedly being anticipated by Karin et al., U.S. Patent No. 6,242,253 (*hereinafter* "Karin"). In view of the remarks put forth below and amendments to the claims, this rejection is respectfully traversed as applied and as it may be applied to the pending claims.

As noted in the specification, "the present invention is based on the discovery of a complementary control mechanism in the nucleus, involving reversible acetylation of the RelA subunit

of NF-κB" (Specification, page 9, paragraph 47). Accordingly, the claimed invention is directed to method for identifying an agent that modulates NF-κB activity in transcription of a gene in a eukaryotic cell **by detecting the level of deactylated RelA**. The methods involve administering a candidate agent and, for example, comparing the level of deactylated RelA in the presence of the candidate agent to the level of deactylated RelA in the absence of the candidate agent.

In contrast, Karin discloses a method for identifying an agent that modulates NF-κB actvity **by detecting the phosphorylated state of IκB-α**. Specifically, Karin discloses methods of screening for modulators of IκB kinases in order to modulate the activity of NF-κB in transcription of a gene. Nowhere does Karin disclose that the level of deacetylated RelA may be examined in order to screen candidate agents for activity in modulating NF-κB transcriptional activity. In fact, as discussed above, the dephosphorylation/phosphorylation of IκB-α is an entirely different regulatory pathway than that of the deactylation/acetylation of RelA.

However, in the spirit of expediting prosecution and without conceding as to the correctness of this rejection, Claim 1 has been amended for clarification to recite "**wherein** the eukaryotic cell **comprises detectably labeled RelA**," and Claim 7 has been amended for clarification to recite "exposing a sample comprising **a detectably labeled** RelA to a test substance."

It is well established that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 2 USPQ 2d 1051, 1053 (Fed. Cir. 1987), cert. denied, 481 U.S. 1052 (1987). See also, Scripps Clinic and Research Foundation v. Genentech, Inc., 18 USPQ 2d 1001 (Fed. Cir. 1991).

Karin fails to disclose the detection of a level of deacteylated RelA in response to exposure to a candidate agent. Moreover, Karin also does not disclose the use of a detectably labeled RelA in order to detect the level of deacetylated RelA. Therefore, Karin fails to anticipate the claimed invention because the cited reference does not teach each and every element as set forth in the claims. Moreover, Karin also fails to teach or suggest examining the level of deactylated RelA with respect to NF-κB transcriptional activity. Instead, Karin focuses on screening for NF-κB modulators by examining the

phosphorylated state of IκB-α, which is an entirely different pathway of NF-κB activation from the acetylation/deacetylation of RelA.

In view of the above, the Applicants respectfully request that the rejection of Claims 1, 4-7, 19-22 under 35 U.S.C. §102(e) be withdrawn.

Rejections Under §102(b)

Claims 1, 4-7, and 19-22 have been rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Traenckner et al., 1994, EMBO J. 13(22)5433-5441 (*hereinafter* "Traenckner"). In view of the remarks put forth below and amendments to the claims, this rejection is respectfully traversed as applied and as it may be applied to the pending claims.

As noted above, the claimed invention is directed to method for identifying an agent that modulates NF-κB activity in transcription of a gene in a eukaryotic cell **by detecting the level of deactylated RelA**.

In contrast, the cited reference discloses observing modulation of NF-κB transcriptional activity by an entirely different pathway. In particular, Traenckner discloses that the proteosome inhibitor PSI stabilizes the phosphorylated form of IκB-α thereby allowing IκB-α to remain bound to NF-κB. Traenckner also discloses that the phosphorylation of IκB-α is necessary for the activation of NF-κB. Accordingly, Traenckner does not disclose or suggest detecting the level of deactylated RelA in order to determine NF-κB activation. The detection of the acetylated or deacteylated state of RelA is completely different than the detection of the phorphorylated state of IκB-α.

However, in the spirit of expediting prosecution and without conceding as to the correctness of this rejection, Claim 1 has been amended for clarification to recite "**wherein** the eukaryotic cell **comprises detectably labeled RelA**," and Claim 7 has been amended for clarification to recite "exposing a sample comprising **a detectably labeled** RelA to a test substance." Support for the amendment can be found in the claims as originally filed, as well as in the specification at, for example: Claim 1: page 15, paragraph 68 through page 16, paragraph 71; and Claim 7: page 17, paragraph 73.

Traenckner fails to disclose the detection of a level of deacteylated RelA in response to exposure to a candidate agent. In addition, Traenckner also does not disclose the use of a **detectably labeled RelA** in order to detect the level of deacetylated RelA. Therefore, Traenckner fails to anticipate the claimed invention because the cited reference does not teach each and every element as set forth in the claims. Moreover, Traenckner also fails to teach or suggest examining the level of deactylated RelA with respect to NF-κB transcriptional activity. Rather, Traenckner discloses examining the phosphorylated state of IκB-α with respect to NF-κB transcriptional activity, which is an entirely different pathway of NF-κB activation.

In view of the above, the Applicants respectfully request that the rejection of Claims 1, 4-7, 19-22 under 35 U.S.C. §102(b) be withdrawn.

Rejections Under §112, Second Paragraph

Claim 22 has been rejected under 35 U.S.C. §112 second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. In particular, the Office Action states that Claim 22 is vague and indefinite for recitation of "is compared to a level of deactylated RelA in the absence of the candidate agent and the presence of HDAC3." Without conceding to the correctness of the rejection, Claim 22 has been amended to avoid this rejection. Withdrawal of this rejection is respectfully requested.

New Claims

In addition, Applicants note that newly added claims 25 to 42 are free of the art cited in the Office Action dated April 6, 2004.

Claims 25 to 31

New claims 25 to 31 are directed to a method for identifying whether an agent modulates NF-κB activity by contacting a candidate agent with a cell that expresses recombinant RelA and detecting the level of deactylated RelA. Since neither Kerin nor Traenckner discloses or suggests the use of a cell that expresses recombinant RelA, these references cannot anticipate claims 25 to 31 under 35 U.S.C. §102, or render the claims obvious under 35 U.S.C. §103.

Claims 32 to 37

New claims 32 to 37 are directed to a method for identifying whether an agent modulates NF-κB activity by contacting a candidate agent with a cell in the presence of an agent that blocks nuclear export and detecting the level of deactylated RelA binding to IκB-α in the cell nucleus or a nuclear extract. Since neither Kerin nor Traenckner discloses or suggests detection of RelA binding in cell nucleus or in a nuclear extract, these references cannot anticipate claims 25 to 31 under 35 U.S.C. §102, or render the claims obvious under 35 U.S.C. §103.

Claims 38 to 42

New claims 38 to 42 are directed to a method for identifying whether an agent modulates NF-κB activity by contacting a candidate agent with a cell then contacting the cell with an antibody that specifically binds acetylated RelA, wherein the binding of the antibody indicates a level of acetylated RelA. Since both Kerin and Traenckner only disclose detection of RelA binding to IκB-α in the cytoplasm, and neither reference discloses or suggests detection of of RelA binding to IκB-α in the nucleus or a nuclear extract, the references cannot anticipate claims 32 to 37 under 35 U.S.C. §102, or render the claims obvious under 35 U.S.C. §103.

Conclusion

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-234.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: July 1, 2004

By: _____
Carol L. Francis
Registration No. 36,513

BOZICEVIC, FIELD & FRANCIS LLP
200 Middlefield Road, Suite 200
Menlo Park, CA 94025
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

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